

Citation:

Colombo J, Kannass KN, Shaddy J, Kundurthi S, Maikranz JM, Anderson CJ, Blaga OM, Carlson SE. Maternal DHA and the development of attention in infancy and toddlerhood. *Child Development*. 2004;75(4):1254-1276.

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Study Design:

Randomized Controlled Trial

Class:

A - [Click here](#) for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine the relationship between docosahexaenoic acid (DHA) levels and the development of attention measured through visual habituation during the first year of life and on measures of attention span and distraction during the second year.

Inclusion Criteria:

Infants were recruited from a previous study on the effects of DHA supplementation on pregnancy length. The follow-up sample was representative of the larger group.

Exclusion Criteria:

None noted by author.

Description of Study Protocol:**Recruitment**

70 infants were recruited for a longitudinal follow-up study from a total of 350 infants and mothers enrolled in a study on the effects of DHA supplementation on pregnancy length. The follow-up sample was representative of the larger group; it did not vary from the larger sample on any of the demographic or medical variables taken.

Design: Randomized Controlled Trial

- Infants were initially enrolled in a randomized, double-blind controlled clinical trial for the evaluation of DHA supplementation on pregnancy outcomes. Mothers' DHA intake was manipulated by providing eggs during the last trimester of pregnancy. All mothers received

eggs and recorded the number they ate but were blinded to whether they were receiving high-DHA (135 mg DHA per egg) or ordinary (35mg DHA per egg) eggs.

- In the follow-up study, participants were seen at 4, 6, and 8 months of age for infant controlled visual habituation sessions augmented with heart-rate (HR) measures.
- Infants were then seen at 12 and 18 months of age for free-play sessions in which looking to objects was measured during a single-object session and in which distractibility was measured during both single- and multiple-object exploration sessions.

Blinding used (if applicable)

Researchers were blinded to which infants were from the original supplemented DHA group or the control group. The blind was broken at the point of the 18-month assessment, but experimenters and observers coding tapes from the final session were in fact functionally blind to the infants' experimental condition and DHA status.

Intervention (if applicable)

- During pregnancy, mothers received high DHA or ordinary eggs, during the last trimester.

Statistical Analysis

- Descriptive statistics were used to determine potential covariates of high- and low- maternal DHA groups.
- MANOVAS were used to analyze the developmental course of look durations and age at 4, 6 and 8 months and maternal DHA, heart-rate defined phases of attention and age and maternal DHA, look duration and age at 12 months and 18 months and maternal DHA, attentional state, age at 12 and 18 months and maternal DHA.

Data Collection Summary:

Timing of Measurements

- Participants were seen at 4, 6, and 8 months of age for infant controlled visual habituation sessions augmented with heart-rate (HR) measures.
- Infants were then seen at 12 and 18 months of age for free-play sessions in which looking to objects was measured during a single-object session and in which distractibility was measured during both single- and multiple-object exploration sessions.

Dependent Variables

- Habituation sessions (4, 6, and 8 months of age)
- Toddler attention assessments (12 and 18 months)

Independent Variables

- Maternal consumption of high DHA, or normal DHA, eggs during last trimester of pregnancy
- Maternal and infant red blood cell phospholipid DHA

Control Variables

Description of Actual Data Sample:

Initial N: 70 infants (27 female) were recruited from a total of 350 infants and mothers enrolled in a previous study. 32 infants (55.1%) were from the supplemented group in the original study.

Attrition (final N): 50 of the 70 infants (71%) provided valid data at each of the three time points for the infant-controlled habituation sessions. 58 infants returned for the 12-month session and 49 toddlers returned for the 18-month session.

Age: Gestation length 39.29 ± 2.24 weeks

Ethnicity: African American 54 (77.1%), Asian American 0, Hispanic 1 (1.4%), Caucasian 15 (21.4%)

Other relevant demographics:

- Apgar score (1 minute) 7.94 ± 1.62
- Apgar score (5 minutes) 8.80 ± 0.67
- Mother's education (yr) 11.77 ± 1.18
- Father's education 11.88 ± 1.37

Anthropometrics

- Birth weight (g) 3248.57 ± 393.02
- Length (cm) 50.60 ± 2.29
- Head circumference (cm) 33.74 ± 1.38

Location: Kansas, US

Summary of Results:

Key Findings:

- Infants whose mothers had high DHA at birth showed an accelerated decline in looking over the first year and increases in examining during single-object exploration and less distractibility in the second year.
- Findings were consistent with evidence suggesting a link between DHA and cognitive development in infancy.
- An Age (4, 6, and 8 months) x DHA (high vs. low maternal DHA) mixed-design multivariate analyses of variance (MANOVA) was performed on the peak look duration from the habituation sessions. A significant main effect emerged for age, $F(2,47)=7.32$, $p<0.01$ as the duration of peak look declined with age.
- The two-way interaction attained significance, $F(2, 47)=3.55$, $p<0.05$. Infants in the high-maternal DHA group showed an accelerated developmental pattern in looking from 4 to 6 months of age relative to the low-maternal DHA group although by 8 months of age the groups were equivalent.
- Analyses on the attention and distractibility data during toddlerhood consistently suggest that toddlers of mothers with higher levels of DHA at birth showed more mature developmental profiles on single-object attention measures and more optimal performance on distractibility assessments than toddlers from mothers with lower DHA.

Look Duration

- An age (4, 6, and 8 months) x DHA (high vs. low maternal DHA) MANOVA found a

significant main effect for age, $F(2, 47)=7.32$, $p<0.01$, as the duration of peak look declined with age.

- The two-way interaction attained significance, $F(2, 47)=3.55$, $p<0.05$.

Heart-rate defined phases of attention (4, 6 and 8 months)

- The main effect of age attained statistical significance ($p<0.001$) for each attentional phase. Significant main effects emerged for DHA group for percentage of time looking.

Maternal DHA and single-object attention (12, 18 months)

- The average length of time looking to the target toy revealed a significant age x maternal DHA interaction, $F(1, 45)=4.56$, $p<0.05$.
- The percentage of turns to distractor was analyzed and found a significant main effect of age, $F(1, 37)=7.08$, $p<0.05$, and a marginally significant main effect of attentional state $F(1, 37)=2.82$, $p=0.10$. There was a marginal effect of maternal DHA, $F(1, 37)=3.37$, $p=0.07$; toddlers of high DHA mothers tended to turn less frequently to the distractor.

Author Conclusion:

In summary, the current results are concordant with mounting evidence of associations between DHA and the status of cognitive function in infancy and early childhood. As noted earlier, future work should seek to document these effects within a more causal framework. Two points should be addressed with specific priority: the first would be the demonstration that maternal DHA can be affected by supplementation during pregnancy, either through a longer period or through a higher dosage of supplementation. The second would be an investigation as to why infant DHA levels were not predictive of infant postnatal outcomes; this is the second study in which this finding has been reported and therefore it appears to be a phenomenon worthy of investigation.

Reviewer Comments:

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	Was the research question clearly stated?	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	Was the selection of study subjects/patients free from bias?	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	Were study groups comparable?	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	Was method of handling withdrawals described?	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes

4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	Was blinding used to prevent introduction of bias?	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	Were outcomes clearly defined and the measurements valid and reliable?	Yes

7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	Was the statistical analysis appropriate for the study design and type of outcome indicators?	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	Are conclusions supported by results with biases and limitations taken into consideration?	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	Is bias due to study's funding or sponsorship unlikely?	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes

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